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NEWS 2
NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks
                 (ROSPATENT) added to list of core patent offices covered
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status
                 data from INPADOC
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enhanced
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new
NEWS 15 APR 04 EMBASE - Database reloaded and enhanced
NEWS 16 APR 18 New CAS Information Use Policies available online
NEWS 17 APR 25 Patent searching, including current-awareness alerts (SDIs),
                 based on application date in CA/CAplus and USPATFULL/USPAT2
                 may be affected by a change in filing date for U.S.
                 applications.
                 Improved searching of U.S. Patent Classifications for
NEWS 18 APR 28
                 U.S. patent records in CA/CAplus
                 GBFULL enhanced with patent drawing images
NEWS 19 MAY 23
                 REGISTRY has been enhanced with source information from
NEWS 20 MAY 23
                 CHEMCATS
NEWS 21 MAY 26
                 STN User Update to be held June 6 and June 7 at the SLA 2005
                 Annual Conference
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             JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
              STN Operating Hours Plus Help Desk Availability
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=>

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chain nodes :
11 19 20 21 22
ring nodes :
chain bonds :
7-11 11-12 19-20 20-21 21-22
ring bonds :
1-2^{-} 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
exact/norm bonds :
7-11 11-12 21-22
exact bonds :
19-20 20-21
normalized bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
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G1:0,S,N,SO2

Hydrogen count :
9:= exact 1
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=> d 11 L1 HAS NO ANSWERS L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful

FULL SEARCH INITIATED 17:19:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 23311 TO ITERATE

100.0% PROCESSED 23311 ITERATIONS

76 ANSWERS

SEARCH TIME: 00.00.01

L2 76 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 161.33 161.54

FULL ESTIMATED COST

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FILE COVERS 1907 - 3 Jun 2005 VOL 142 ISS 24 FILE LAST UPDATED: 2 Jun 2005 (20050602/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12 L3 4 L2

=> d 13 1- ibib abs hitstr YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:120821 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

140:163886

TITLE:

Preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases

Gazit, Aviv; Levitzki, Alexander

PATENT ASSIGNEE(S):

Yissum Research Development Company of the Hebrew

University of Jerusalem, Israel

SOURCE:

GI

PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PA	PATENT NO.						KIND DATE				ICAT:	DATE					
WO	2004013091				A2 20040212			1	70 2	003-		20030731					
WO	2004	2004013091				A3 20040729											
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		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
		PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	TN,
		TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
							CM,										-
PRIORIT	PRIORITY APPLN. INFO.:										002-		P 20020801				
OTHER S	MARPAT 140:163886								(1							

 $(R^3)_n \xrightarrow{l}$

AB Title compds. I [R1 = (un) substituted Ph, naphthyl, etc.; R2 = H, halo, phenylamino, etc.; R3 = H, alkoxy, NO2, etc.; n = 1-3] are prepared For instance, 4-chloro-6-methylquinazoline is reacted with 2-aminophenol (EtOH, reflux, 1 h) to give II. I are potent inhibitors of protein tyrosine (PTK) kinase activity, particularly epidermal growth factor receptor (EGFR) kinase activity. I are useful in treating a variety of PTK related disorders such as cell proliferative disorders, fibrotic disorders, metabolic disorders and cancer.

IT 655248-61-6P, 3-[2-Bromo-4-((6,7-dimethoxyquinazoline-4-yl)amino)phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]acrylamide 655248-62-7P, N-Benzyl-3-[2-bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyanoacrylamide 655248-63-8P, 3-[2-Bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyano-N-(4-yl)amino-N-(4-yl)am

CN

phenylbutyl)acrylamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

RN 655248-61-6 CAPLUS

2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

655248-62-7 CAPLUS

RN

CN 2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 655248-63-8 CAPLUS

CN 2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-(4-phenylbutyl)- (9CI) (CA INDEX NAME)

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228866 CAPLUS

DOCUMENT NUMBER: 134:266317

Preparation of quinazolines as aurora 2 kinase TITLE:

inhibitors

Mortlock, Andrew Austen; Keen, Nicholas John; Jung, INVENTOR(S):

Frederic Henri; Brewster, Andrew George Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 306 pp.

CODEN: PIXXD2

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	ΑТ	ENT N	10.			KIND DATE					APPL	ICAT		DATE						
w	10	20010		A1 20010329			,	WO 2	000-		2	0000	918							
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																	GM,			
																	LS,			
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,		
			SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,		
			YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM						
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			DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,		
			CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG					
С	Ά	2384291					AA 20010329				CA 2000-2384291						0000	918		
В	BR	20000		A 20020521				BR 2000-14116						2	20000918					
E	ĽΡ	1218354				A 1		2002	0703		EP 2	000-		20000918						
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,		
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J	JP 2003509499					T2 20030311					JP 2	001-		20000918						
, E	EE 200200119					Α		2003	0415		EE 2	002-		20000918						
		10649	92			A 20030131				BG 2002-106492						2	20020307			
Z	ZA 2002002234					A 20030619			0619	ZA 2002-2234						2	0020	319		
N	NO 2002001399					Α		2002	0430		NO 2	002-	1399			2	0020	320		
PRIORI	TY	APP	LN.	INFO	.:						GB 1	999-	2215	4		A 1	9990	921		
											GB 1	999-	2217	0		A 1	9990	921		
											WO 2	000-	GB35	80		W 2	0000	918		

OTHER SOURCE(S): MARPAT 134:266317

GI

$$R^{1}$$
 R^{2}
 R^{3}
 R^{4}
 R^{6}
 R^{7}
 R^{7}
 R^{7}
 R^{8}
 R^{8}
 R^{8}
 R^{6}
 R^{6}

Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR12; R12 = H or AB alkyl; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R13, or R15X1; R13 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, CO2, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R15 = H or (un) substituted hydrocarbyl, heterocyclyl, or alkoxy; R5 = NHCO2R9, NHCOR9, NHSO2R9, COR9, CO2R9, SOR9, SO2OR9, CONR10R11, SONR10R11, or SO2NR10R11; R9-R11 = independently H or (un) substituted hydrocarbyl or heterocyclyl; or R10 and R11 together with the N to which they are attached = (un) substituted heterocyclyl; R6 = H or (un) substituted hydrocarbyl or heterocyclyl; R7 and R8 = independently H, halo, alkyl, (di)alkoxy(methyl), alkanoyl, CF3, CN, NHY2, alkenyl, alkynyl, or (un) substituted Ph, PhCH2, or heterocyclyl; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, a 7-step sequence involving (1) alkylation of morpholine with 1-bromo-3-chloropropane (49%), (2) addition of Et vanillate to yield Et 3-methoxy-4-(3morpholinopropoxy)benzoate (100%), (3) nitration (86%), (4) reduction to the amine using 10% Pd/C (100%), (5) cycloaddn. with formamide to form the quinazoline(68%), (6) chlorination to give 4-chloro-6-methoxy-7-(3morpholinopropoxy) quinazoline (60%), and (7) amination with N-benzoyl-4-aminoaniline (58%) yielded II. The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration

II

0.0193 μ M. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.06 μ M and reduced BrdU incorporation into cellular DNA by 50% at 0.159-0.209 μ M.

331776-88-6P

of

IT

RN

CN

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 4-substituted quinazoline aurora 2 kinase inhibitors for treatment of cancer and other proliferative diseases) 331776-88-6 CAPLUS

2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228865 CAPLUS

DOCUMENT NUMBER: 134:266316

TITLE: Preparation of quinazoline derivatives, method of

preparation and use in inhibiting aurora 2 kinase

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	PATENT NO.						DATE	APPLICATION NO.							DATE						
WO	2001		A1 200			0010329							2	0000	918						
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		LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX	, M	ΙΖ,	NO,	NZ,	PL,	PT,	RO,	RU,			
							SL,														
							BY,														
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		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT	', L	U,	MC,	NL,	PT,	SE,	BF,	ВJ,			
		CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR	R, N	ΙE,	SN,	TD,	TG						
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EP	1218357				A1 20020703				EΡ	200	00-9	9626		2	20000918 20000918						
EP	1218				B1 20050406										20000918 20000918 20000918 SE, MC, PT,						
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	R, I	Τ,	LI,	LU,	NL,	SE,	MC,	PT,			
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JP	JP 2003509498					T2 20030311					200	1-!	5249		20000918						
EE	EE 200200148					A 20030415					200	2-:		20000918							
AT	AT 292628					E 20050415					AT 2000-962682							20000918			
ZA	2002	0018	31		A 20030605			0605	ZA 2002-1831							20020305					
NO	NO 2002001395						20020515										0020	320			
BG	BG 106535						2002	1229		BG	200	2-2	1065	35		2	0020	320			
PRIORIT	IORITY APPLN. INFO.:									GB	199	9-2	2217	3		A 1	9990	921			
										WO	200	0-0	GB35	62	1	₩ 2	0000	918			
OTHER SO	HER SOURCE(S):					PAT	134:	2663	16												

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB I or a salt, ester, amide or prodrug thereof, a method for the preparation of I and the use of the claimed compds. for inhibiting aurora 2 kinase are claimed. These compds. are useful in the treatment of cancer. In I: X is O, or S, S(O) or S(O)2 or NR10 where R10 is H or C1-6 alkyl. R5 is OR11, NR12R13 or SR11 where R11, R12 and R13 are independently optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R12 and R13 may addnl. form together with the N atom to which they are attached, an optionally substituted aromatic or nonarom. heterocyclic ring which may contain further heteroatoms. R6 and R7 are independently H or hydrocarbyl. R8 and R9 are independently H, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkoxymethyl, di(C1-4alkoxy)methyl, C1-4 alkanoyl, trifluoromethyl, cyano, amino, C2-5 alkenyl, C2-5 alkynyl, a Ph group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms,

selected independently from O, S and N, which heterocyclic group may be aromatic or nonarom. and may be saturated (linked via a ring C or N atom) or unsatd. (linked via a ring C atom), and which Ph, benzyl or heterocyclic group may bear on one or more ring C atoms up to 5 substituents selected from hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C2-4 alkanoyl, C1-4 alkanoylamino, C1-4 alkoxycarbonyl, C1-4 alkylthio, C1-4 alkylsulfinyl, C1-4 alkylsulfonyl, carbamoyl, N-C1-4alkylcarbamoyl, N,N-di(C1-4alkyl) carbamoyl, aminosulfonyl, N-C1-4alkylaminosulfonyl, N,N-di(C1-4alkyl)aminosulfonyl, C1-4 alkylsulfonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C1-4alkoxycarbonyl. R1, R2, R3, R4 are independently halo, cyano, nitro, C1-3 alkylthio, -N(OH)R14 (R14 is H, or C1-3 alkyl), or R16X1- (X1 represents a direct bond, -O-, -CH2-, -OC(O)-, -C(O)-, -S-, -SO-, -SO2-, -NR17C(O)-, -C(O)NR18-, -SO2NR19-, -NR20SO2- or -NR21- (R17, R18, R19, R20 and R21 each independently represents H, C1-3 alkyl or C1-3alkoxyC2-3alkyl), and R16 is H, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy). A method for preparing I comprises reacting II where X, R8 and R9 are as defined above, R1', R2', R3', R4' are groups R1, R2, R3, R4 as defined above resp., or precursors thereof; and R85 is a leaving group, with HCR6:CR7C(0)R5', where R6 and R7 are as defined above, R5' is a group R5 as defined above or a precursor group therefore; and thereafter if desired or necessary, converting any precursor groups R1', R2', R3', R4' or R5' to groups R1, R2, R3, R4 or R5 resp., or changing a group R5 to a different such group. The compds. of the invention inhibit the serine/threonine kinase activity of the aurora 2 kinase and thus inhibit the cell cycle and cell proliferation. Procedures for assessing these properties are described and test results are given for (E)-4-[4-(2-(3-methylcyclohexylaminocarbonyl)ethenyl)anilino]-6,7dimethoxyquinazoline.

IT 331734-29-3p, (E)-4-[4-(2-Carboxyethenyl)anilino]-6,7dimethoxyquinazoline 331734-31-7p, (E)-4-[4-(2Carboxyethenyl)anilino]-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline
hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(intermediate; preparation of quinazoline derivs., method of preparation

in inhibiting aurora 2 kinase)

RN 331734-29-3 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-31-7 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, hydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●x HCl

IT 331733-89-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of quinazoline derivs., method of preparation and use in inhibiting

aurora 2 kinase)

RN 331733-89-2 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 331733-38-1P 331733-40-5P 331733-41-6P 331733-43-8P 331733-44-9P 331733-46-1P 331733-48-3P 331733-50-7P 331733-52-9P 331733-53-0P 331733-55-2P 331733-57-4P 331733-59-6P 331733-61-0P 331733-64-3P 331733-78-8P 331733-79-0P 331733-80-3P

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    331733-84-7P 331733-85-8P 331733-86-9P
    331733-87-0P 331733-88-1P 331733-90-5P
    331733-91-6P 331733-92-7P 331733-93-8P
    331733-94-9P 331733-95-0P 331733-96-1P
    331733-97-2P 331733-98-3P 331733-99-4P
    331734-00-0P 331734-01-1P 331734-02-2P
    331734-03-3P 331734-04-4P 331734-05-5P
    331734-06-6P 331734-07-7P 331734-08-8P
    331734-09-9P 331734-10-2P 331734-11-3P
    331734-12-4P 331734-13-5P 331734-14-6P
    331734-15-7P 331734-16-8P 331734-17-9P
    331734-19-1P 331734-20-4P 331734-21-5P
    331734-22-6P 331734-23-7P 331734-24-8P
    331734-25-9P 331734-26-0P 331734-27-1P,
     (E)-4-[4-(2-Carboethoxyethenyl)anilino]-6,7-dimethoxyquinazoline
    331734-28-2P, (E)-4-[4-(2-Carboethoxyethenyl)phenoxy]-6,7-
    dimethoxyquinazoline
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of quinazoline derivs., method of preparation and use in
inhibiting
       aurora 2 kinase)
     331733-38-1 CAPLUS
     2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-phenyl-
     , (2E) - (9CI) (CA INDEX NAME)
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Double bond geometry as shown.

RN 331733-40-5 CAPLUS
CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-ethyl-,
(2E)- (9CI) (CA INDEX NAME)

RN 331733-41-6 CAPLUS

CN Morpholine, 4-[(2E)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-1-oxo-2-propenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-43-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(4-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-44-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(1,3-dimethylbutyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-46-1 CAPLUS

CN 2-Propenamide, N-[(2-chlorophenyl)methyl]-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-48-3 CAPLUS

CN 2-Propenamide, N-(2,3-dihydroxypropyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-50-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylpropyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-52-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-53-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxyethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-55-2 CAPLUS

CN 2-Propenamide, N-(cyanomethyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-57-4 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-[3-(dimethylamino)propyl]-, (2E)- (9CI) (CA INDEX NAME)

MeO
$$\frac{N}{N}$$
 $\frac{E}{N}$ $\frac{H}{N}$ $\frac{NMe_2}{N}$

CN 2-Propenamide, N-butyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-61-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxy-1-methylethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-64-3 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-68-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methylcyclohexyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-71-2 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-75-6 CAPLUS

CN 2-Propenamide, N-(4-chlorotetrahydro-1,1-dioxido-3-thienyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-77-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-[(5-methyl-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-79-0 CAPLUS

CN 2-Propenamide, N-cyclopropyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-80-3 CAPLUS

CN 2-Propenamide, N-cyclobutyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-81-4 CAPLUS

CN 2-Propenamide, N-cyclopentyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-82-5 CAPLUS
CN 2-Propenamide, N-cyclohexyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-83-6 CAPLUS

CN Piperidine, 1-[(2E)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-1-oxo-2-propenyl]- (9CI) (CA INDEX NAME)

RN 331733-84-7 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-85-8 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-86-9 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-87-0 CAPLUS

CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-88-1 CAPLUS

CN 2-Propenamide, N-(4-chlorophenyl)-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-90-5 CAPLUS

CN 2-Propenamide, N-(cyclohexylmethyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$N$$

RN 331733-91-6 CAPLUS

CN 2-Propenamide, N-(6-chloro-3-pyridinyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-92-7 CAPLUS

CN 2-Propenamide, N-(2-furanylmethyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$O$$

$$O$$

RN 331733-93-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[(tetrahydro-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$O$$

RN 331733-94-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-2-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$
 $(CH_2)_3$
 $(CH_2)_3$

RN 331733-95-0 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331733-96-1 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

RN 331733-97-2 CAPLUS

CN 2-Propenamide, N-(1,3-dimethylbutyl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$(CH_2)_3$$
 MeO
 HN
 E
 H
 N
 $Bu-i$
 O
 Me

RN 331733-98-3 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2,2,2-trifluoroethyl)-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$
 $(CH_2)_3$
 $(CH_2)_3$

RN 331733-99-4 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylpropyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-00-0 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$N$$

$$Pr-n$$

RN 331734-01-1 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-02-2 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$MeO$$

$$HN$$

$$E$$

$$HN$$

RN 331734-03-3 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[2-(2-thienyl)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-04-4 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[(5-methyl-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

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PAGE 1-B

[─]Me

RN 331734-05-5 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(tetrahydro-1,1-dioxido-3-thienyl)-, (2E)-(9CI) (CA INDEX NAME)

$$(CH_2)_3$$
 $(CH_2)_3$
 $(CH_2)_3$

RN 331734-06-6 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[2-(methylthio)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-07-7 CAPLUS

CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

RN 331734-08-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[2-(methylthio)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-09-9 CAPLUS

CN 2-Propenamide, N-cyclopentyl-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-10-2 CAPLUS

CN 2-Propenamide, N-cyclohexyl-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-11-3 CAPLUS

CN 2-Propenamide, N-(cyclohexylmethyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-12-4 CAPLUS

CN 2-Propenamide, N-(6-chloro-3-pyridinyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-13-5 CAPLUS

CN 2-Propenamide, N-(2-furanylmethyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-14-6 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[(tetrahydro-2-furanyl)methyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-15-7 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-3-pyridinyl-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-16-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-17-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2,2,2-trifluoroethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-19-1 CAPLUS

CN 2-Propenamide, N-(2,3-dihydroxypropyl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

RN 331734-20-4 CAPLUS
CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-21-5 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(3-methylcyclohexyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-22-6 CAPLUS

CN 2-Propenamide, N-(2,3-dihydro-1H-inden-2-yl)-3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-23-7 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-[2-(2-thienyl)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-24-8 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(tetrahydro-1,1-dioxido-3-thienyl)-, (2E)-(9CI) (CA INDEX NAME)

RN 331734-25-9 CAPLUS

CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(phenylmethyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-26-0 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 331734-27-1 CAPLUS

CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

RN 331734-28-2 CAPLUS
CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228864 CAPLUS

DOCUMENT NUMBER: 134:252355

TITLE: Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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OTHER SOURCE(S): MARPAT 134:252355

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$$R^{2}$$
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AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; Ra = (un)substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 4-phenoxyaniline•HCl and 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.069 μM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 2.89 μM and reduced BrdU incorporation into cellular DNA by 50% at 3.68 μM.

II

IT 330999-73-0

RN

CN

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of 4-substituted quinazoline aurora 2 kinase inhibitors for treatment of cancer and other proliferative diseases)
330999-73-0 CAPLUS

2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

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